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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,091	11/25/2003	Jose Remacle	4044.001	7897

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5 and 7-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5 and 7-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/8/2008 has been entered.

Status of Claims

Claims 1, 4-5 and 7-21 are pending and under examination.

Withdrawn Rejections

In view of the amendments to the claims, the 35 USC 112 first and second paragraph rejections have been withdrawn. Also, the 103 rejection over Devereaux is withdrawn in view of applicant's arguments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1, 4-5 and 7-21, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo (Faming Zhuanli Shenqing Gongkai) in view of Stillman (20030175827) or Sanford (US 2003/0134294).

Guo discloses throughout the article, e.g., in the abstract a method in which a protein chip with array of 10-10,000 cm-1 and array size of 5-500 consists of the activated carrier and spotting solution. The spotting solution is composed of probe (such as antigen, antibody, drug receptor, agglutinin, cell, or tissue), fucose, antiseptic (such as Na azide) and C2-10 aliphatic polyol. The protein chip is manufactured by spotting the mixture of probe and spotting solution on the activated carrier sheet, and then blocking with bovine serum. The protein chip may be used to detect, recognize, and identify the antigen, antibody, medicine or its receptors, polysaccharide, agglutinin, tissue, or cell. See further, pages 12-13; paragraph bridging pages 16 and 17. Guo discloses the used of saccharide as C2-C10 alkyl (liner, as claimed) polyalcohol, not the claimed species mannitol, maltitol or sorbitol. However, it would have been obvious to pick and choose any one of the species included in the C2-C10 alkyl polyalchol taught by Guo and as similarly

claimed. These species are known in the art as evident from teachings of e.g., Stillman.

Stillman teaches throughout the patent at e.g., paragraph [0026] referring to FIG. 3;

> A series of compositions were tested including….antibody protein. The difference amongst the solutions was the saccharide used, namely, glucose, ***mannitol***, xylose, trehalose, maltodextrin, and glucuronic acid. Spotted and dried solution spots were tested for shelf life, i.e., the retention of biological activity, in this case, a specific binding reaction. While some saccharides delivered a higher specific signal than others, all delivered a signal at least twice that of the control solution which did not contain any saccharide.

See the similar teachings of Sandord below.

As held by the majority in Merck & Co. Inc. v. Biocraft Laboratories, Inc., 874 F.2d 804, 10 USPQ 2d 1843 (Fed. Cir. 1989), at 10 USPQ 2d 1846:

> That the '813 patent discloses a multitude of effective combinations(herein only in the C2-C7 range) does not render any particular formulation less obvious. This is especially true because the claimed composition (herein the saccharide e.g., sorbitol) is used for the identical purpose taught by the prior art. See In re Corkill, 771 F.2d 1496, 1500, 226 USPQ 1005, 1008 (Fed. Cir. 1985) (obviousness rejection of claims affirmed in light of prior art teaching that "hydrated zeolites will work" in detergent formulations, even though "the inventors selected the zeolites of the claims from among "thousands of compounds"); In re Susi, 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971) (obviousness rejection affirmed where the disclosure of the prior art was "huge, but it undeniably include[d] at least

> some of the compounds recited in appellants generic claims and it is of a class of chemicals to be used for the same purpose as appellant's additives").

Claims 1, 4-5 and 7-21, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over either Stillman (20030175827) or Decker(GB 2,016,687A) in combination with either Guo or Sandford (US 2003/0134294) and Schultz et al(20040198637) as reiterated below.

Stillman discloses at paragraph [0010] a method for producing a thin film dried protein composition comprising making a protein containing solution that is to be dried on a surface, preferably a biologically active protein. The term "biologically active" includes any protein that can participate in a specific binding reaction, (such as antibodies, antibody fragments, antigens, antigen fragments), as well as peptides or enzymes.) The solution is made with a buffer that maintains the surface pH between about 5.0 and 9.0 during solution drying and with a saccharide in an amount sufficient to stabilize the protein during solution drying. The solution is then applied to a support having the surface for depositing. Thin film of protein containing solution is allowed to dry on the support surface under normal pressures. At paragraph [0011] the method enables one to make stable thin film dried protein compositions.

Such films can be incorporated into protein analytical devices. of particular interest are proteomic microarrays.

Stillman further discloses at e.g., paragraph [0026] referring to FIG. 3;

> A series of compositions were tested including a PBS/5% trehalose/10% methanol solution containing 1.5 mg/ml of antibody protein. The difference amongst the solutions was the saccharide used, namely, glucose, ***mannitol***, xylose, trehalose, maltodextrin, and glucuronic acid. Spotted and dried solution spots were tested for shelf life, i.e., the retention of biological activity, in this case, a specific binding reaction. While some saccharides delivered a higher specific signal than others, all delivered a signal at least twice that of the control solution which did not contain any saccharide.

Decker discloses at e.g., pages 2 up to 5 an immunoassay method for the detection and determination of antigens and antibodies. The method comprises an indirect application of an antibody or antigen to a solid support (a selected capture protein, as claimed). It generally involves the procedure in which the solid support is precoated with antigen or antibody to potentiate the adherence of the antibody or antigen. The reagents consist of a solid support that has been coated either directly or indirectly with an antigen or antibody and stabilized with a sugar coating to impart a storage capability. The percent of sugar e.g., xylitol, mannitol and sorbitol is given in Table II.

Stillman and Decker do not disclose the use of antiseptic as sodium azide and that the protein is covalently linked to the solid support. However, Guo discloses throughout the article, e.g., in the abstract a method in which a protein chip with array of 10-10,000 cm-1 and array size of 5-500 consists of the activated carrier and spotting solution. The spotting solution is composed of probe (such as antigen, antibody, drug receptor, agglutinin, cell, or tissue), fucose, antiseptic (such as Na azide) and C2-10 aliphatic polyol. The protein chip is manufactured by spotting the mixture of probe and spotting solution on the activated carrier sheet, and then blocking with bovine serum. The protein chip may be used to detect, recognize, and identify the antigen, antibody, medicine or its receptors, polysaccharide, agglutinin, tissue, or cell. See further, e.g., pages 12-13; paragraph bridging pages 16 and 17.

Sandford discloses at paragraph [0197] that preservatives like azide are effective to retard or prevent microbial proliferation. Sandford discloses at paragraph [0199] that lyoprotectants are effective to reduce or prevent chemical or physical instability of a protein upon lyophilization and storage. Examples of a polyol such as trihydric or higher sugar alcohol (e.g., glycerin, erythritol, glycerol, arabitol,

xylitol, sorbitol, and mannitol). Sandford also discloses the use of borate buffer.

Schultz et al discloses:

> [0101] In one embodiment, the polypeptides are provided in a reaction mixture that is suitable for the necessary reaction between the reactive group on the unnatural amino acid side chain and the reactive group attached to the solid support. ….. In some embodiments, the polypeptides remain hydrated throughout the preparation, storage, and assaying of the array to prevent denaturation of the polypeptide. Accordingly, humectants or polymers such as glycerol, polyethylene glycol, glycerin, **maltitol**, polydextrose, sorbitol, cetyl alcohol, fatty alcohols, propylene glycol, and the like, can be used to prevent evaporation of the nanodrops.
>
> [0048] Systems for immobilizing polypeptides on a solid support, as well as the resulting solid supports containing the polypeptides, e.g., protein arrays, are provided. The systems allow one to covalently or non-covalently attach the polypeptides to the solid support in such a manner as to preserve the function of the polypeptides or to regain their functionality once attached. The ***covalent or non-covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.).*** The protein arrays of the invention are versatile and can be adapted to a variety of protein analysis formats. The arrays find use in a wide variety of applications, including numerous types of screening protocols and any protein analysis where high throughput parallel analysis is desirable.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use azide in the method of either Decker or Stillman as taught by either Sandford or Guo. The advantages taught by Sandford or

Guo would provide the motivation to one having ordinary skill in the art as to the known use of azide as a preservative. Note that Guo discloses C2-C10 alkyl polyalcohol instead of the now claimed xylitol or mannitol. However, it would be within the ordinary skill in the art at the time the invention was made to pick the specific saccharide within the given range taught by Guo as evidenced by Decker or Stillman and as claimed. Furthermore, as taught by Schultz the protein can be covalently or non-covalently link to the array in a manner that preserves its function.

Response to Arguments

Applicant acknowledges that Schultz provides protein arrays where a polypeptide is attached to a solid support, and where the polypeptide incorporates at least one unnatural amino acid and the polypeptide is attached to the solid support by a chemical linkage that is formed from the reaction product between a first reactive group that is on the side chain of the unnatural amino acid and a second reactive group that is attached to a solid support. Schultz, paragraph [0008]. The purpose of Schultz's invention is to provide specific covalent bonding between only the unnatural amino acid and a reactive group on the solid surface. One skilled in the art would

understand that Schultz does not teach employment of a reactive group on the solid surface that will form a covalent bond with a natural amino acid; this would sacrifice the specificity that is the goal of Schultz.

In reply, applicant's arguments are not commensurate in scope with the claims. The claims do not preclude unnatural amino acids. Rather, broad natural and unnatural amino acids. See e.g., claim 4 which recites unnatural D-enantiomer amino acids. Nonetheless, as stated by Schultz above:

> The ***covalent or non-covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.).***

Attention is further directed to Schultz at e.g., paragraph [0060]:

> …. one of the reactive groups is an electrophilic moiety, and the second reactive group is a nucleophilic moiety. Either the nucleophilic moiety or the electrophilic moiety can be attached to the side chain of the unnatural amino acid. That reactive group is then used in a reaction that couples the polypeptide to the solid support. Suitable electrophilic moieties that react with nucleophilic moieties to form a covalent bond are known to those of skill in the art. Such electrophilic moieties include, but are not limited to, e.g., carbonyl group, a sulfonyl group, an aldehyde group, a ketone group, a hindered ester group, a thioester group, a stable imine group, an epoxide group, an aziridine group, etc.

Cf. with paragraph [0044] of the instant disclosure cited by applicant in the instant REMARKS.

Thus, it would be within the ordinary skill in the art to determine which site forms the covalent binding between the capture amino acid containing protein and the reactive group in the solid surface.

Applicant recognizes that Sandford teaches covalent binding between proteins and active groups in a hydrogel matrix. However, Applicant claims binding between an amino group and a solid surface, not a gel matrix.

In reply, the claims do not preclude a gel matrix surface. The claim as broadly written encompasses any type of solid surface.

Applicant submits there was no motivation to combine the cited references above and below. Applicants cite different case laws to support their arguments.

In reply, the court in KSR v. Teleflex, 17 S. Ct. 1727, 82 USPQ 2d 1385 (2007) states:

> The diversity of inventive pursuits and of modern technology counsels against confining the obviousness analysis by a formalistic conception of the words teaching, suggestion, and **motivation**… and the explicit content of issued patents. In many fields there may be little discussion of obvious techniques or combinations, and market demand, rather than scientific literature, may often drive design trends. Granting patent protection to advances that would occur in the ordinary course

without real innovation retards progress and may, for patents combining previously known elements, deprive prior inventions of their value or utility. Since the TSM test was devised, the Federal Circuit doubtless has applied it in accord with these principles in many cases. There is no necessary inconsistency between the test and the Graham analysis. But a court errs where, as here, it transforms general principle into a rigid rule limiting the obviousness inquiry. Pp. 14-15.

(c) The flaws in the Federal Circuit's analysis relate mostly to its narrow conception of the obviousness inquiry consequent in its application of the TSM test. The Circuit first erred in holding that courts and patent examiners should look only to the problem the patentee was trying to solve. Under the correct analysis, any need or problem known in the field and addressed by the patent can provide a reason for combining the elements in the manner claimed. Second, the appeals court erred in assuming that a person of ordinary skill in the art attempting to solve a problem will be led only to those prior art elements designed to solve the same problem……. It is common sense that familiar items may have obvious uses beyond their primary purposes, and a person of ordinary skill often will be able to fit the teachings of multiple patents together like pieces of a puzzle….. When there is a design need or market pressure to solve a problem and there are a **finite number of identified, predictable solutions**, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Pp. 15-18.

Applicant argues that Stillman teaches the use of denaturing surfaces, which are likely to diminish the capture protein's activity. It would not be obvious to modify the invention of Stillman to create the Applicant's invention, because Stillman's method involves denaturing the protein, and the goal of the Applicant's invention is to preserve the protein in its native conformation. Because Stillman's use of denaturing

surfaces will denature the proteins' native conformation, Stillman teaches away from the Applicant's invention.

In reply, applicant's arguments are not commensurate in scope with the claims. The claims merely recite capture protein, which can read on denatured or native protein.

Applicant requests the Examiner reconsider his declination to provide an English translation of Guo.

In reply, the unavailability of the translation does not mean declination to provide the English version. Nonetheless, enclosed is the English translation of the Guo reference. Applicant argues that the purpose of Sandford is to provide a stable hydrogel matrix to which biological materials are immobilized (covalently bound) in a hydrated three-dimensional hydrogel matrix. Sandford assures the preserved activity of the biological material by immobilizing the biological material in the semi-aqueous medium of the hydrogel. Sandford's invention is directed to keeping proteins in an aqueous environment, and points out the need to prevent drying (see particularly paragraph [0274] of Sandford, in which a step is taken to prevent drying). The structure of a hydrogel matrix is destroyed upon drying. The claimed embodiments teach a method of preserving activity upon drying, whereas Sandord teaches a

method of preventing drying in the first place. If Sandford were modified as the Examiner suggests, then the invention of Sandford would be useless for its intended purpose.

In response, Sanford is not employed for the purpose as argued. Rather for its teachings of using preservatives like azide effective to retard or prevent microbial proliferation of a protein upon storage.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/T. D. Wessendorf/

Primary Examiner, Art Unit 1639